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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte DURLIN HICKOK, ROBERT HUSSA,
MARK FISCHER-COLBRIE, EMORY V. ANDERSON,
and ANDREW E. SENYEI

Appeal 2010-004671
Application 10/774,144
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and
MELANIE L. McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a screening and treating method. The Examiner has rejected the claims as

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

non-enabled, lacking written description, indefinite, and obvious. We have jurisdiction under 35 U.S.C. § 6(b). As to at least one rejection of each claim, we affirm.

STATEMENT OF THE CASE

Claims 67-94 are pending and on appeal (App. Br.[2] 2-3). We will focus on claim 67, which reads as follows:

> 67. A method of screening and treating a subject, comprising: a) obtaining a sample from a subject who is asymptomatic for preterm or imminent delivery; b) detecting a fetal restricted antigen in said sample from said subject and assessing whether the level of fetal restricted antigen is indicative of a risk of preterm or imminent delivery; and c) if the level of fetal restricted antigen is indicative of the risk, administering a progestational agent to the subject, whereby delivery is delayed.

The other claims discussed herein are set forth in Appendix A to the Amended Appeal Brief (App. Br. 15-19).

Claims 67-76, 79, and 81-94 stand rejected under 35 U.S.C. § 112, first paragraph, for lacking enablement (Ans.[3] 5).

Claims 67-94 stand rejected under 35 U.S.C. § 112, first paragraph, for lacking written description (Ans. 6).

Claims 67-94 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite (Ans. 7).

Claims 67-76 and 79-94 stand rejected under 35 U.S.C. § 103(a) as obvious over Leavitt[4] in view of Johnson,[5] Meis,[6] or Keirse[7] and further in view of Weiner[8] or Andersen[9] (Ans. 9).

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[2] "App. Br." refers to the Amended Appeal Brief dated March 20, 2009.
[3] "Ans." refers to the Examiner's Answer dated November 12, 2009.
[4] Leavitt et al., WO 94/17405 A1, Aug. 4, 1994.

Claims 77 and 78 stand rejected under 35 U.S.C. § 103(a) as obvious over Leavitt in view of Johnson, Meis, or Keirse, further in view of Weiner or Andersen, and additionally in view of Allen[10] or Olsen[11] (Ans. 11).

ENABLEMENT

The Examiner finds:

> The prior art would suggest that an ability to prolong a pregnancy at risk for preterm delivery is not a property known or common to the generic list (see pages 10-12) of progestational agents disclosed by appellant. . . . Many agents are considered to be progestational on the basis of pharmacological tests, yet the results of the use of progestational agents, such as progesterone-related agents, generally for prolonging a pregnancy at risk for preterm delivery . . . would seem unknown and unpredictable because only specific agents were tested and suggested to have that ability. . . . Random experimentation unguided by appellant to determine progestational agents that do or do not function in the invention suggested by appellant's specification is undue experimentation. Absent further guidance from appellant, and

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[5] Johnson et al., *Efficacy of 17α-Hydroxyprogesterone Caproate in the Prevention of Premature Labor*, 293 NEJM 675-680 (1975).
[6] Meis, *17 Alpha Hydroxyprogesterone Caproate Prevents Recurrent Preterm Birth*, 187 AM. J. OBSTET. GYNECOL. S54 (2002).
[7] Keirse, *Progestogen administration in pregnancy may prevent preterm delivery*, 97 BR. J. OBSTET. GYNECOL. 149-154 (1990).
[8] Weiner et al., *The therapeutic efficacy and cost-effectiveness of aggressive tocolysis for premature labor associated with premature rupture of the membranes*, 159 AM. J. OBSTET. GYNECOL. 216-222 (1988).
[9] Andersen & Merkatz, *Preterm Labor*, in DANFORTH'S OBSTETRICS AND GYNECOLOGY, chap. 17, pp. 335-351 (6th ed. 1990).
[10] Allen & Harris, *The Role of n-3 Fatty Acids in Gestation and Parturition*, 226 EXP. BIOL. MED. 498-506 (2001).
[11] Olsen et al., *Randomized controlled trial of effect of fish-oil supplementation on pregnancy duration*, 339 LANCET 1003-1007 (1992).

> such random unguided undue experimentation, one would not be assured of the ability to practice the invention commensurate in scope with these claims.

(Ans. 5-6.)

Issue

Has the Examiner set forth a prima facie case that the Specification does not enable the full scope of progestational agents recited in claim 67?

Findings of Fact

1. The Specification states that "the term 'progestational agent' refers to any agent that favors, or is conducive to, gestation" (Spec. 10).

2. The Specification discloses that "[p]rogestational agents include any of a group of hormones normally secreted by the corpus luteum and placenta, and in small amounts by the adrenal cortex, whether naturally or synthetically produced, and derivatives thereof" (*id.*).

3. The Specification also discloses that "[a]mong progestational agents are progesterone-related agents, which refer to a member of a group of steroid compounds that are progesterones or progesterone derivatives that retain progesterone activity *that inhibits or delays delivery*" (*id.* at 10-11 (emphasis added)).

4. In addition, the Specification, referring to Spicer,[12] provides a list of "[e]xemplary progestational agents for use in accord with the methods herein," the list including, among many others, 17α-hydroxyprogesterone (*id.* at 11).

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[12] Spicer et al., US 5,211,952, May 18, 1993.

5. The Specification also discloses: "Progestational agents also include omega-3 fatty acids, whether naturally or synthetically produced, and derivatives thereof. Exemplary omega-3 fatty acids include, for example, docosahexaenoic acid (DHA). Progestational agents include gestagens, progestagens, progestins, progestogens, and progestational hormones." (*Id.*)

6. Spicer is directed to method for inhibiting conception comprising administering a gonadotropin releasing hormone "composition at a dose sufficient to completely suppress ovarian steroid production, in combination with a precisely formulated regimen of add-back steroids," including a progestational steroid (Spicer, col. 1, ll. 6-13, & col. 3, ll. 26-52).

7. Spicer provides a list of progestational agents that can be used in its invention, which substantially overlaps with the list set forth in the Specification (*compare* Spicer, col. 6, ll. 46-52, to Spec. 11).

8. Peters[13] discloses that 15,16-seco-19-nor progestins "possess potent progestational activity" (Peters, col. 1, ll. 20-25).

9. Peters also discloses administering its compounds to achieve the desired progestational effect, such as suppressing ovulation (*id.* at col. 5, ll. 26-29, & col. 9, ll. 24-30).

Principles of Law

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the

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[13] Peters et al., US 5,321,044, Jun. 14, 1994.

specification of the application." *In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993).

Enablement does not require testing every species encompassed by a claim, even in an unpredictable art. *See In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976). Instead, "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991) (footnote omitted).

Analysis

The Specification states that "the term 'progestational agent' refers to any agent that favors, or is conducive to, gestation" (Finding of Fact (FF) 1). The Specification discloses a broad range of progestational agents (FF 2-5). The Examiner has not set forth sufficient basis to doubt the assertion that a broad range of progestational agents may be used.

The Examiner argues:

> Appellant has provided nothing on the record to predictably link the use of a generic progestational agent, such as those progesterone-related agents or other agents listed in the specification, as a contraceptive (i.e., preventing a pregnancy, as in Spicer . . . or Peters . . .) to its successful use as an agent for prolonging a pregnancy at risk for preterm delivery.

(Ans. 5-6.) Peters does disclose administering 15,16-seco-19-nor progestins to achieve the desired progestational effect, such as suppressing ovulation (FF 8-9). In addition, Spicer discloses administering progestational agents, together with a gonadotropin releasing hormone, to inhibit conception (FF 6). However, we do not agree that the Examiner has adequately shown that these references support the Examiner's position that undue

experimentation would have been required to practice the full scope of the invention.

The Examiner also finds that "appellant's specification provides no working examples of pregnancy prolongation other than that demonstrated in the art with progesterone (da Fonseca et al.) or 17α-hydroxyprogesterone (Johnson et al., Yemini et al., Keirse, or Meis et al.) or omega-3 fatty acid supplementation (Allen et al. or Olsen et al.)" (Ans. 6). However, the Examiner has not adequately explained why these examples, together with the other disclosures in the Specification, are insufficient to enable the full scope of claim 67.

Conclusion

The Examiner has not set forth a prima facie case that the Specification does not enable the full scope of progestational agents recited in claim 67. We therefore reverse the enablement rejection of claims 67-76, 79, and 81-94.

WRITTEN DESCRIPTION

The Examiner finds that "the specification, as originally filed, does not provide support for the patient population as is now claimed" (Ans. 6). In particular, the Examiner finds that "Appellant provides no written description that only patients with risk factors not including symptoms should be tested to the exclusion of those with symptoms as is now claimed" (*id.* at 7). In addition, the Examiner finds that "appellant does not define, and one would not readily know absent further guidance from appellant, what patients are encompassed by the current criteria of 'asymptomatic' because only a short inclusive list of possible symptoms is taught" (*id.*).

Issue

Has the Examiner set forth a prima facie case that the Specification does not describe conducting the method on a subject who is asymptomatic for preterm or imminent delivery?

Findings of Fact

10. The Specification states that, "[d]ue to the subtlety of symptoms associated with preterm delivery, many subjects are not diagnosed as having an increased risk of preterm delivery until later in their pregnancies" (Spec. 1).

11. The Specification also states:

> The present methods can be used on any pregnant woman following about 12 weeks, about 16 weeks, or about 20 weeks gestation. In addition to screening any woman to determine whether delivery is imminent, the subjects who should be screened are those subjects with clinically intact membranes in a high risk category for preterm delivery, and especially, those women whose pregnancies are not sufficiently advanced to ensure delivery of a healthy fetus.

(*Id.* at 18.)

12. In addition, the Specification states:

> [T]here are a large number of factors known to be associated with the risk of preterm delivery. Those factors include, but are not limited to, multiple fetus gestations; incomplete cervix; uterine anomalies; polyhydramnios; nulliparity; previous preterm rupture of membranes or preterm labor; preeclampsia; first trimester vaginal bleeding; little or no antenatal care; and *symptoms such as abdominal pain, low backache, passage of cervical mucus and contractions*. Any pregnant woman at about 12 or more weeks gestation with clinically intact membranes and having one or more risk factors for preterm delivery should be tested throughout the risk period; i.e., until

> about 37 weeks gestation. Risk factors for spontaneous abortion include gross fetal anomalies, abnormal placental formation, uterine anomalies and maternal infectious disease, endocrine disorder cardiovascular renal hypertension, autoimmune and other immunologic disease, and malnutrition.

(*Id.* at 18-19 (emphasis added).)

Principles of Law

"In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). Nonetheless, the disclosure must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. *See id.*

Analysis

The Specification discloses that the "present methods can be used on any pregnant woman following about 12 weeks, about 16 weeks, or about 20 weeks gestation" (FF 11). In particular, the Specification discloses that "the subjects who should be screened are those subjects with clinically intact membranes in a high risk category for preterm delivery" (FF 11). In addition, the Specification discloses that "factors known to be associated with the risk of preterm delivery" include symptoms, as well as other factors that are not symptoms (FF 12). We agree with Appellants that these teachings clearly convey that Appellants were in possession of the concept of using the method on a subject who is asymptomatic for preterm or imminent delivery. In addition, the Examiner has not shown that one of ordinary skill in the art would not know what patients are encompassed by the claim recitation of asymptomatic for preterm or imminent delivery.

Conclusion

The Examiner has not set forth a prima facie case that the Specification does not describe conducting the method on a subject who is asymptomatic for preterm or imminent delivery. We therefore reverse the written description rejection of claims 67-94.

INDEFINITENESS

The Examiner finds various recitations in the claims to be indefinite (Ans. 8).

Issue

Has the Examiner set forth a prima facie case that these various recitations are indefinite?

Principles of Law

"A claim is indefinite if its legal scope is not clear enough that a person of ordinary skill in the art could determine whether a particular composition infringes or not." *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003).

Analysis

We note initially that the failure to enter an amendment is a petitionable matter. Thus, we will not decide whether the Examiner was within his rights in failing to enter the amendment.

In addition, we agree with the Examiner that claims 81 and 83 are indefinite. In particular, we find claim 81 to be indefinite because "'the' therapeutically effective amount lacks antecedent basis" and we find claim 83 to be indefinite because "it is not clear if 'the' sample is the same sample tested in claim 67 or a newly obtained sample" (Ans. 8).

However, with regard to the other recitations alleged to be indefinite, we conclude that the Examiner has not provided adequate basis for these determinations. For example, claim 67 recites "the level" twice. Although the first recitation of "the level" does not have antecedent basis, we do not agree that one of ordinary skill in the art would not understand what "the level" refers to in the context of the claim. Instead, we find that one of ordinary skill in the art would understand that it refers to the level detected in the first phrase of step b.

Conclusion

The Examiner has set forth a prima facie case that claims 81 and 83 are indefinite. However, the Examiner has not set forth adequate basis to reject claims 67-80, 82, and 84-94 on this basis. We therefore affirm the indefiniteness rejection of claims 81 and 83 and reverse the indefiniteness rejection of claims 67-80, 82, and 84-94.

OBVIOUSNESS

With regard to the obviousness rejections, the claims subject to each rejection have not been argued separately and therefore the claims set forth in each ground of rejection stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii).

The Examiner relies on Leavitt for disclosing the "determination[] of fetal fibronectin (i.e. a fetal restricted antigen . . .) . . . as [a] biochemical marker[] of impending imminent preterm delivery and of insulin-like growth factor binding protein-1 to determine fetal membrane status to aid clinical decisions regarding administration of treatments to prolong pregnancy in pregnant patients at 12 to 37 weeks gestation" (Ans. 9).

The Examiner also finds that "[a]ny of Johnson . . . , Meis . . . , or Keirse . . . teach the efficacy of progesterone treatments in reducing preterm delivery" (*id.*).

In addition, the Examiner finds:

> Weiner et al. or Andersen et al. teach that treatment with tocolytic agents is not beneficial (Weiner et al.) and not recommended (Andersen et al., page 346; Weiner et al.) in patients with rupture of membranes. Progestational agents are known as among the tocolytic agents that function to prevent or reduce contractions prior to preterm labor (see e.g. Andersen et al. (page 345)).

(Ans. 9-10.)

The Examiner concludes that it would have been obvious

> to have tested a pregnant patient determined to have biochemical markers indicative of impending preterm delivery for the status of the fetal membranes and to treat those patients with intact fetal membranes indicated as at risk of having impending delivery with a pregnancy-prolonging agent . . . , such as the progesterones as taught by any of Johnson et al., Meis et al., or Keirse.

(*Id.* at 10.)

The Examiner additionally relies on Allen or Olsen for disclosing omega-3 fatty acid, as recited in dependent claims 77 and 78 (*id.* at 11).

Appellants argue that "[n]owhere in Leavitt *et al.*, Johnson *et al.*, Meis *et al.*, Keirse, Weiner *et al.* or Anderson *et al.*, either alone or in combination, is there any teaching or suggestion of testing and treating an asymptomatic patient" (App. Br. 12). With regard to the rejection of claims 77 and 78, Appellants additionally argue that Allen and Olsen do not overcome this deficiency (*id.* at 13).

Issue

Does the evidence support the Examiner's conclusion that it would have been obvious to conduct the method on a subject who is asymptomatic for preterm or imminent delivery?

Findings of Fact

13. Leavitt discloses "an assay that distinguishes those patients with impending imminent delivery with intact membranes from those in whom the membranes have ruptured" (Leavitt 3: 29-32).

14. Leavitt also discloses:

> [T]he method comprises obtaining a cervicovaginal secretion sample from a pregnant patient after about week 20 of gestation and determining the level of fetal fibronectin and IGFBP-I in the sample. The presence of an elevated fibronectin level in the sample indicates an increased risk of imminent delivery. . . . For those patients whose fetal fibronectin assay result indicates an increased risk of preterm delivery, the test of the patient's IGFBP-I level determines whether the membranes are intact. If the test for IGFBP-1 is negative, the patient can be treated to prolong the pregnancy.

(*Id.* at 4: 5-26.)

15. In addition, Leavitt discloses:

> In addition to screening any woman to determine whether delivery is imminent, the patients who should be tested for a delivery indicator, are those patients with clinically intact membranes in a high risk category for preterm delivery, and preferably, all those women whose pregnancies are not sufficiently advanced to ensure delivery of a healthy fetus.

(*Id.* at 6: 1-8.)

16. Leavitt also discloses:

> Ninety percent of the fetal morbidity and 100 percent of the fetal mortality associated with preterm delivery is for those fetuses delivered prior to 32 to 34 weeks gestation. Therefore, 32 to 34 weeks gestation is an important cutoff for the health of the fetus, and women whose pregnancies are at least about 20 weeks and prior to 34 weeks in gestation should be tested.

(*Id.* at 6: 8-15.)

17. In addition, Leavitt discloses:

> [T]here are a large number of factors known to be associated with the risk of preterm delivery. Those factors include multiple fetus gestations; incompetent cervix; uterine anomalies; polyhydramnios; nulliparity; previous preterm rupture of membranes or preterm labor; preeclampsia; first trimester vaginal bleeding; little or no antenatal care; and *symptoms such as abdominal pain, low backache, passage of cervical mucus and contractions*. Any pregnant woman at 12 or more weeks gestation with clinically intact membranes and having one or more risk factors for preterm delivery should be tested throughout the risk period; i.e., until about week 37. Risk factors for spontaneous abortion include gross fetal anomalies, abnormal placental formation, uterine anomalies and maternal infectious disease, endocrine disorder cardiovascular renal hypertension, autoimmune and other immunologic disease, and malnutrition.

(*Id.* at 6: 16-34 (emphasis added).)

Analysis

Leavitt discloses testing "women whose pregnancies are at least about 20 weeks and prior to 34 weeks in gestation" (FF 16). Leavitt also discloses that, "[i]n addition to screening any woman to determine whether delivery is imminent, the patients who should be tested for a delivery indicator, are those patients with clinically intact membranes in a high risk category for

preterm delivery" (FF 15). In addition, Leavitt discloses that "factors known to be associated with the risk of preterm delivery" include symptoms, as well as other factors that are not symptoms (FF 17). Thus, we agree with the Examiner that Leavitt suggests screening a subject who is asymptomatic.

Conclusion

The evidence supports the Examiner's conclusion that it would have been obvious to conduct the method on a subject who is asymptomatic for preterm or imminent delivery. We therefore affirm the obviousness rejections of claims 67 and 77. Claims 68-76 and 79-94 fall together with claim 67. Claim 78 falls together with claim 77.

SUMMARY

We affirm the obviousness rejections of claims 67-94 and the indefiniteness rejection of claims 81 and 83. However, we reverse the indefiniteness rejection of claims 67-80, 82, and 84-94, as well and the enablement and written description rejections.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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